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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,449	06/22/2005	Benedetta Crescenzi	ITR0046YP	1421

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EXAMINER	
MOORE, SUSANNA	
ART UNIT	**PAPER NUMBER**
1624	

MAIL DATE	DELIVERY MODE
08/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,449	CRESCENZI ET AL.	
	Examiner	Art Unit	
	Susanna Moore	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/24/06, 4/12/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group (III) in the reply filed on 4/12/2007 is acknowledged. The traversal is on the ground(s) that unity of invention exists between Groups (I-IV) because the special technical feature is the fused bicyclic hydroxypyrimidinone carboxamide core and there is no serious search burden. This is not found persuasive because the entire heterocyclic ring system is the feature, as Applicant pointed out. Furthermore, the different heterocyclic ring systems do not belong to the same class. Indeed, each heterocycle has its own name and provides its own class of compounds. The Markush group clearly lacks unity of invention.

The requirement is still deemed proper and is therefore made **FINAL**.

Specification

1. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: SUBSTITUTED PYRIMIDO[1,2-a]AZEPINE AND RELATED COMPOUNDS USEFUL AS HIV INTEGRASE INIHBITORS.

Claim Objections

2. Claim 10 is objected to because of the following informalities: the 79th species is missing a parenthesis. Appropriate correction is required.

Claim Rejections

3. Claims 1-14 and 16 are rejected as drawn to an improper Markush group, as these claims contain both elected and non-elected subject matter, which are parts of different inventions. The choices are not art-recognized equivalents for reasons set forth in the requirement for restriction. Deletion of non-elected subject matter will overcome the rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 2, 12-14 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Regarding claims 1, 2, 12-14 and 16, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are

part of the claimed invention. See MPEP § 2173.05(d). The definition for R4, point 2, 3 and 10 have seven "e.g." throughout.

5. Claims 3 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim s 3 and 5 recite the limitation "SO_2CH_3, or $C(O)NH(CH_3)$" in R4. There is insufficient antecedent basis for this limitation in the claim.

6. Claims 4 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim s 3 and 5 recite the limitation "$N[SO_2N(CH_3)_2]SO_2R^{18}$" and "$N[SO_2N(CH_3)_2]CH_2C(O)N(CH_3)_2$" in R1. There is insufficient antecedent basis for this limitation in the claim.

7. Claims 1, 2, 12-14 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 1 and 9 the variable "HetA" and "heteroaromatic ring" which defines R4 on page 7, "...optionally substituted...oxo." This is impossible; aromatic rings have only one hydrogen on each carbon and oxo requires two hydrogen to replaart to which it pertains, invention of these claims. diseases. The only established prophylactics d]pyrimidine compounds such as present here. 5.

8. Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The therapeutic agents in claim 13 are relative terms, which renders the claim indefinite. The term "HIV protease inhibitor," "non-nucleoside HIV reverse transcriptase" and "nucleoside HIV reverse transcriptase inhibitors" are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprized of the scope of the invention. The nature of the instant invention where the method of use claims consist of the compounds according to claim 1 and an additional active ingredient, i.e. HIV protease inhibitor, which is as a therapeutic agent.

9. Claims 13 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for preventing diseases. The specification does not enable any person skilled in the art with which it is most nearly connected, to use Applicants invention. Applicants are not enabled for "preventing" an infection by HIV or for "preventing... or delaying the onset of AIDS." In addition, it is presumed that "prevention" of the claimed disease would require a method of identifying those individuals who will develop the claimed diseases before they exhibit symptoms. There is no evidence of record that would guide the skilled clinician to identify those who have the potential of becoming afflicted.

The factors to be considered in making an enablement rejection were summarized above. 1) As discussed above, preventing diseases requires identifying those patients who will acquire the disease before Parkinsonism occurs. This would require extensive and potentially opened ended clinical research on healthy subjects. 2) The passages spanning line 14, page 27 to line 23, lists the diseases Applicants intend to treat. 3) There is no working example of such a preventive procedure in man or animal in the specification. 4) The claims rejected are drawn to clinical neurology and are therefore physiological in nature. 5) The state of the art is that no general procedure is art-recognized for determining which patients generally will suffer Parkinson's disease before the fact. 6) The artisan using Applicants invention would be a Board Certified physician in neurological diseases with an MD degree and several years of experience. Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of movement disorders generally. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens, 163 USPQ 609*. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk, 42 USPQ2nd 1001, 1006*. This establishes that it is not reasonable to any agent to be able to prevent movement disorders generally. That is, the skill is so low that no compound effective generally against movement disorders has ever been found let alone one that can prevent such conditions. 7) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). 8)

The claims broadly read on all patients, not just those undergoing therapy for the claimed diseases and on the multitude of compounds embraced by Formula (I). The Examiner suggests deletion of the word "preventing" and the phrase "delaying the onset."

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susanna Moore whose telephone number is (571) 272-9046. The examiner can normally be reached on M-F 8:00-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SM
6/22/07

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